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Tissue and blood collection study from patients who have progressed on a PARP inhibitor (a type of targeted cancer drug)

Submission date 28/10/2022	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 07/12/2022	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 21/01/2025	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The purpose of the study is to collect blood and tumour samples from patients whose cancer has got worse while receiving treatment or following treatment with a drug called a PARP inhibitor, which is used to treat certain types of cancer. The samples will be analysed to help us understand what type of changes have occurred in your cells. This will involve looking at the DNA (DNA carries genetic information and tells cells what proteins to make), RNA (RNA is used by the body to make proteins) and the proteins in the cells that are tested.

We know that certain changes in a person's DNA, RNA or proteins could mean that they may benefit from treatment with a new type of drug that is being developed (called a DNA polymerase theta inhibitor – this is a drug that can stop the repair of damaged DNA and therefore may kill cancer cells). We would like to understand how many people have these changes and if we can detect them. This information should help us to devise the best tests to identify patients who could benefit from this new type of drug that is being developed.
The study is planned to last for up to 2 years.

Who can participate?
Male and female patients aged 18 years and over who have disease progression following treatment with a PARP inhibitor.

What does the study involve?
This is a tissue (blood or tumour biopsy) collection study. Samples will be collected from up to 50patients. We would like to collect the following samples from you, however, if you wish you can decide not to provide the biopsy sample described in point 3 below. You would still be to be able to participate in this study by giving a blood sample only.

Tumour or blood samples that were taken before you started any treatment with a PARP inhibitor and have been stored by the hospital (if they are still available). The sample may be used to look at your DNA, RNA or protein.

A blood sample – this will be collected at the same time as a blood sample is collected from you for routine testing or when your biopsy sample is collected. This will be up to approximately 4 tablespoons of blood. The blood sample will be used for DNA analysis.

A biopsy sample (a small piece of tissue which would be no bigger than the size of a pea) from your tumour. This could be collected during a procedure that is part of your standard care or the biopsy may be collected specifically for this study. The biopsy sample may be used to look at your DNA, RNA or protein.

In addition to the collection of the samples you will also be contacted by telephone 28days after the biopsy sample was taken (if you have agreed to provide this) to find out if you had any side-effects from the procedure.

Information from your medical records and clinical information about your cancer will be recorded for the study.

Your participation in the study will be for up to a maximum of 2months. If you decide to participate in the study, you can choose to leave the study at any time without needing to give a reason.

What are the benefits and risks of participating?
Benefits
There are not expected to be any direct medical benefits to taking part in the study. Patients diagnosed with cancer in the future may benefit from an increased understanding of the type and frequency of changes that occur when a cancer gets worse during treatment, or following treatment with a PARP inhibitor. If we find out that there are changes that could result in improved treatment with another type of drug known as a DNA polymerase theta inhibitor, this will enable us to use this type of drug in the future in a more personalised way. We might be able to predict whether an individual will benefit from receiving the drug. If this is possible it would prevent us from giving the drug to patients who are unlikely to benefit from it.
Risks
If you have a biopsy you may suffer some side-effects from it. The type of side effects you may suffer will depend on the type of biopsy that is performed.

Where a needle biopsy is performed, the tissue is obtained by inserting a needle into the tumour after a smaller needle has been used to inject some medicine to numb your skin called anaesthetic. You may experience a brief sharp pain from the needle used to inject the anaesthetic. The biopsy needle that will remove the sample of your tumour will produce a dull pain. There may be bleeding, bruising, swelling, infection, or scarring at the site of the biopsy. Your doctor may offer you a medicine to calm your nerves and help you to relax before or during the biopsy procedure. You may be given painkillers after the biopsy to help manage any pain.

If the biopsy is collected by inserting a tube through the mouth, nose, rectum or urethra or by surgery you may experience pain and discomfort as a result. Your doctor may use a local anaesthetic or a general anaesthetic during the biopsy procedure. You may be given painkillers after the biopsy to help manage any pain. There is also the rare possibility that serious complications from bleeding or organ damage may occur, and this may result in additional surgery.

Infections can also occur as a result of the biopsy, though the risk is estimated to be less than 1 in 100. If you do develop an infection you may be given antibiotics.

The biopsy may be guided using a CT scan. CT scans are quick, painless and generally safe. But there's a small risk you could have an allergic reaction to the contrast dye used. In rare cases, patients can suffer from kidney problems as a result of this reaction. This CT scan would be extra to those CT scans that you may have as part of your standard care. This procedure uses ionising radiation to form images of your body. Ionising radiation may cause cancer many years or decades after the exposure. The chances of this happening to you as a consequence of taking part in this study are less than 0.14%

During the collection of the blood samples there could be bruising at the site where the needle is inserted. There may also be an inflammation of the vein, infection, redness, pain, bleeding, blood clots (which may cause inflammation, swelling and pain), and nerve damage. The blood samples will be collected in more than one tube.

Where is the study run from?
The study is being carried out at the Sarah Cannon Research Institute UK, Limited

When is the study starting and how long is it expected to run for?
January 2022 to February 2025

Who is funding the study?
The study is funded by Artios Pharma Limited (UK)

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
309701

Protocol serial number
ART4215C004

Study information

Scientific Title
A study to investigate the type and frequency of molecular alterations in the cancers of patients whose disease has undergone clinical progression while receiving treatment or following treatment with a PARP inhibitor for an approved indication.

Acronym
PolQ-ID

Study objectives
The purpose of the ART4215C004 study is to collect tumour and blood samples from patients who have been treated with PARP inhibitors for analysis.. This analysis will help the understanding about the type and frequency of molecular alterations, such as changes to DNA, that can occur when a patient is treated with a PARP inhibitor. We aim to find out if there are changes that could result in patients responding to another drug known as a DNA Polymerase theta inhibitor.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/04/2022, London Central Research Ethics Committee (4 Minshull Street, Manchester M1 3DZ, UK; +44 207 1018143; londoncentral.rec@hra.nhs.uk) ref:22/PR/0114

Primary study design
Observational

Study design
Multicenter observational sample collection study

Study type(s)
Other

Health condition(s) or problem(s) studied
Cancer patients whose disease has undergone clinical progression while receiving treatment or following treatment with a PARPi for an approved indication.

Interventions
Each patient must participate in the informed consent process and sign and date an informed consent form (ICF) for this protocol before any protocol-required procedures are performed. Participants will be given an information sheet to consider usually for at least 24 hours and the research team will arrange to discuss the study with the potential participants to ensure patients understand the commitment required to fulfil the study requirements. During the consent process, patients will be made aware that participation is voluntary and they can leave the study at any time without their standard care being affected.

Patients with available archival post-PARPi tumour samples and/or liquid biopsy samples who are not able to provide a new biopsy or who are deceased may be identified by the clinical team and registered for the study if the patient previously provided generic research consent for use of clinical data and tissue/blood samples.

A solid tumour biopsy and/or blood samples will be collected after the time of progression and will be used to characterise the patient’s cancer at the genomic, transcriptomic and protein level. The biopsy sample(s) will be collected within 28 days of signing informed consent. The investigator will assess if the patient is suitable for a biopsy. The site of biopsies and type of biopsies will be personalized based on tumour location, tumour burden and other patient

characteristics. The method used to obtain a percutaneous biopsy (ultrasound guided, CT guided, punch biopsy, etc) will be based on tumour location.

Circulating tumour DNA (ctDNA) will be extracted from whole blood and also analysed by genomic sequencing. Blood samples will be taken at the same time as standard of care bloods or collection of the biopsy sample, within 28 days of signing informed consent.

Archival tumour tissue from any site and any timepoint before PARPi initiation will be retrieved if available from patients who provide a tumour biopsy post progression on a PARP inhibitor. Where multiple timepoints of pre-PARPi archival samples exist, the sample taken chronologically closest to pre-PARPi initiation will be prioritised.

The study will recruit up to 3cohorts of patients.
Cohort1: Patients who have experienced disease progression while receiving treatment or following treatment with a PARP inhibitor (PARPi) for an approved indication or during a clinical trial and who are willing to provide a new biopsy or blood samples.
Cohort2: Patients with available archival post-PARPi tumour samples and/or a liquid biopsy sample who are not able to provide a new biopsy may be identified by the clinical team and registered for the study if the patient previously provided generic research consent for use of clinical data and tissue/blood samples.
Cohort3: Patients with available archival post-PARPi tumour samples and/or liquid biopsy samples who are deceased may be identified by the clinical team and registered for the study if the patient previously provided generic research consent for use of clinical data and tissue /blood samples.

Intervention Type
Other

Primary outcome(s)
1. DNA extracted from tumour samples will be analysed by Whole Exome Sequencing (WES) for copy number variations (CNV), as well as gene fusions, single nucleotide variations (SNVs) and insertions and deletions (indels).
2. ctDNA extracted from whole blood will be analysed for CNV, as well as gene fusions, SNVs and indels by Next Generation Sequencing (NGS).

Key secondary outcome(s)
Current secondary outcome measures as of 14/02/2024:
1. Tumour samples will be analysed by ribonucleic acid (RNA) sequencing (RNASeq), immunohistochemistry (IHC), or other suitable methods which can be used to assess transcriptomic or proteomic alterations.
2. The incidence and nature of transcriptomic or proteomic alterations will be assessed.
3. ctDNA: Assessment of DNA sequence analysis to determine the incidence of BRCA1 and BRCA2 reversions.

Previous secondary outcome measures:
1. Tumour samples will be analysed by ribonucleic acid (RNA) sequencing (RNASeq), RNAscope, immunohistochemistry (IHC), or other suitable methods which can be used to assess transcriptomic or proteomic alterations.
2. The incidence and nature of transcriptomic or proteomic alterations will be assessed.
3. ctDNA: Assessment of DNA sequence analysis to determine the incidence of BRCA1 and BRCA2 reversions.

Completion date
16/02/2025

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Provide signed written informed consent for this study (Cohort 1). Patients with archival tissue who are not able to provide a new biopsy (Cohort 2) or deceased patients (Cohort 3) must have provided generic research consent for use of clinical data and tissue/blood samples.
2. ≥18 years of age.
3. Histologically- or cytologically-confirmed diagnosis of cancer.
4. Have cancer that has undergone disease progression while receiving treatment or following treatment with a PARPi for an approved indication or within a clinical trial. (Note at the discretion of the Sponsor patients may have received a subsequent treatment following disease progression during or following treatment with a PARPi). Patients may have received PARPi treatment in combination with another treatment.
For Cohort 1 only:
5. Willing to provide either a core biopsy from a tumour lesion that has exhibited progression on or after PARPi treatment and that is deemed suitable for imaging-guided biopsy (ultrasound or computed tomography [CT]) by an experienced radiologist or suitable for intra-operative biopsy during secondary debulking surgery as determined by an experienced oncology surgeon and a blood sample for WES, and/or a blood sample for ctDNA analysis.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
20

Key exclusion criteria
1. Discontinued PARPi for toxicity within 2 months of starting PARPi.
For Cohort 1 only:
2. For patients requiring a new biopsy, have a significant bleeding disorder or coagulopathy that in the investigator’s opinion would increase the risk associated with study biopsy.
3. Any other severe concurrent disease which may increase the risk associated with study

participation.
4. Any psychological, familiar, sociological or geographical considerations potentially hampering compliance with the study and follow up schedule.

Date of first enrolment
01/11/2022

Date of final enrolment
01/03/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Sarah Cannon Research Institute UK, Limited
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Sponsor information

Organisation
Artios Pharma Limited

Funder(s)

Funder type
Industry

Funder Name
Artios Pharma Limited

Results and Publications

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date.
The data arising will belong to the trial sponsor Artios.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No